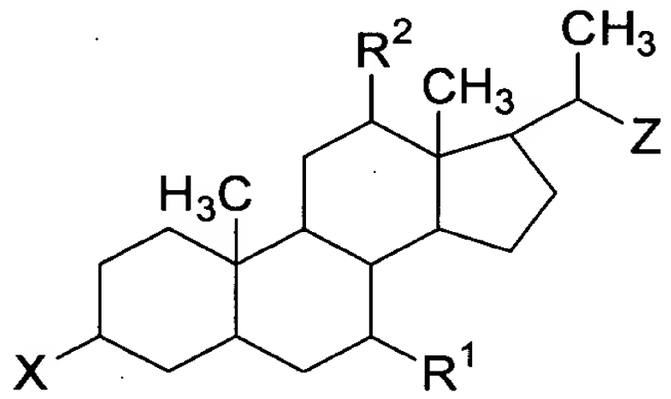
CLAIM SUMMARY DOCUMENT

1. (Currently Amended) A method for achieving sustained therapeutic or prophylactic blood concentrations of a GABA analog or an active metabolite thereof in the systemic circulation of an animal which method comprises orally administering to said animal a compound of formula (I):



(I)

a1

wherein:

R^1 and R^2 are independently hydrogen or hydroxy;

X is ~~selected from the group consisting of~~ hydroxy ~~and D–Q^a–(T)– wherein:~~

~~T is –O– or –NH–~~;

~~Q^a is a covalent bond or a linking group that may cleave under physiological conditions to release a GABA analog or active metabolite thereof into the systemic blood circulation of said animal, wherein said linking group is not a linear oligopeptide comprising 1, 2 or 3 α-amino acids and/or β-amino acids; and~~

~~D is a GABA analog moiety~~

Z is ~~selected from the group consisting of (a) a substituted alkyl group containing a moiety which is negatively charged at physiological pH which moiety is selected from the group consisting of –COOH, –SO$_3$H, –SO$_2$H, –P(O)(OR^{19})(OH), –OP(O)(OR^{19})(OH), –OSO$_3$H, wherein R^{19} is selected from the group consisting of alkyl, substituted alkyl, aryl and substituted aryl; and (b)~~ a group of the formula:

$$–M–Q^b–D'$$

wherein:

M is selected from the group consisting of $-CH_2OC(O)-$ and $-CH_2CH_2C(O)-$;

Q^b is a covalent bond or a linking group of formula:

$$-[E-(F^*)_n-G]_m-$$

wherein:

m is an integer of from 1 to 4;

n is 0 or 1;

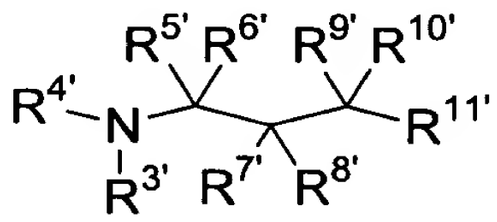
E is –NH- or –O-;

F* is selected from a group consisting of alkylene, substituted alkylene, alkenylene, substituted alkenylene, alkynylene, substituted alkynylene, cycloalkylene, substituted cycloalkylene, cycloalkenylene, substituted cycloalkenylene, arylene, substituted arylene, heteroarylene, substituted heteroarylene, heterocyclene and substituted heterocyclene; and

G is -OC(O)-, -C(O)-, or –NH-;

wherein Q^b ~~which~~ is cleavable ~~may cleave~~ under physiological conditions ~~to release a GABA analog or active metabolite thereof into the systemic blood circulation of said animal, wherein said linking group~~ provided that Q^b is not a linear oligopeptide consisting of 1, 2 or 3 α-amino acids and/or β-amino acids; and

D' is a GABA analog moiety of the formula:



wherein:

$R^{3'}$ is a covalent bond linking the GABA analog moiety to Q^b;

$R^{4'}$ is hydrogen or $R^{4'}$ and $R^{9'}$ together with the atoms to which they are attached form a heterocyclic ring;

$R^{5'}$ and $R^{6'}$ are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, aryl, substituted aryl, heteroaryl and substituted heteroaryl;

$R^{7'}$ and $R^{8'}$ are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, alkynyl, aryl, substituted aryl, heteroaryl and substituted heteroaryl, or $R^{7'}$ and $R^{8'}$ together with the atoms to which they are attached form a cycloalkyl, substituted cycloalkyl, heterocyclic or substituted heterocyclic ring;

$R^{9'}$ is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, alkynyl, aryl, substituted aryl, heteroaryl and substituted heteroaryl;

$R^{10'}$ is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, alkynyl, aryl, substituted aryl, heteroaryl and substituted heteroaryl;

$R^{11'}$ is selected from the group consisting of carboxylic acid, carboxylic amide, carboxylic ester, sulfonamide, phosphonic acid, acidic heterocycle, sulfonic acid, and hydroxamic acid; or

a pharmaceutically acceptable salt thereof.

~~provided that when X is hydroxy, then Z is a group of the formula –M–Q^b–D'.~~

2. (Canceled)

3. (Original) The method according to Claim 1 wherein

R^1 and R^2 are both α-OH; or

R^1 is β-OH and R^2 is hydrogen; or

R^1 is α-OH and R^2 is hydrogen; or

R^1 is hydrogen and R^2 is α-OH; or

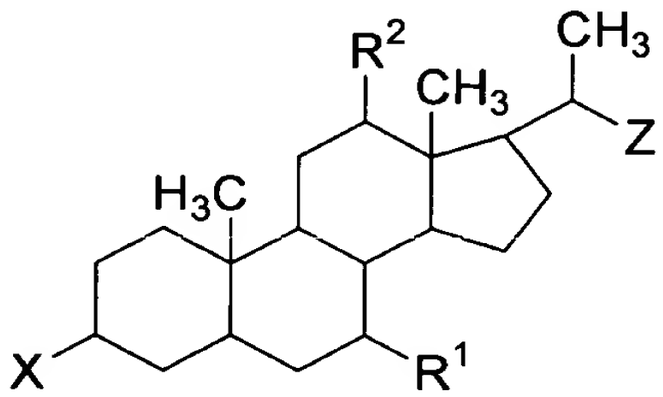
R^1 is β-OH and R^2 is α-OH; or

R^1 and R^2 are both hydrogen.

4. (Currently Amended) The method according to Claim 1 ~~2~~ wherein ~~D–Q^a–(T)– and/or~~ –M-Q^b-D' is ~~are~~ selected to cleave under physiological conditions at a rate to provide a therapeutic and/or prophylactic blood concentration of the GABA analog or active metabolite thereof in the animal for a period of at least about 10% longer than

when the GABA analog is orally delivered by itself at an equivalent dose.

5. (Currently Amended) A compound of formula (I):



(I)

wherein:

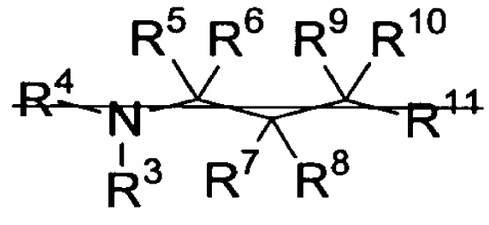
R^1 and R^2 are independently hydrogen or hydroxy;

X is ~~selected from the group consisting of~~ hydroxy ~~and D-Q^a-(T)- wherein:~~

~~T is -O or -NH-~~;

~~Q^a is a covalent bond or a linking group; and~~

~~D is a GABA analog moiety preferably of the formula:~~



~~where:~~

~~R^3 is selected from the group consisting of hydrogen, an amino protecting group, or a covalent bond linking the GABA analog moiety to Q^a;~~

~~R^4 is hydrogen, or R^4 and R^9 together with the atoms to which they are attached form a heterocyclic ring;~~

~~R^5 and R^6 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, aryl, substituted aryl, heteroaryl and substituted heteroaryl;~~

~~R^7 and R^8 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, alkynyl, aryl, substituted aryl, heteroaryl and substituted heteroaryl, or R^7 and R^8 together with the atoms to which they are attached form a cycloalkyl, substituted cycloalkyl, heterocyclic or substituted heterocyclic ring;~~

~~R^9 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, alkynyl, aryl, substituted aryl, heteroaryl and substituted heteroaryl;~~

~~R^{10} is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, alkynyl, aryl, substituted aryl, heteroaryl and substituted heteroaryl;~~

~~R^{11} is selected from the group consisting of carboxylic acid, carboxylic amide, carboxylic ester, sulfonamide, phosphonic acid, acidic heterocycle, sulfonic acid, hydroxamic acid and $C(O)R^{12}$;~~

~~R^{12} is a covalent bond linking the GABA analog moiety to Q^a, provided only one of R^3 and R^{12} links D to Q^a;~~

Z is ~~selected from the group consisting of (a) a substituted alkyl group containing a moiety which is negatively charged at physiological pH which moiety is selected from the group consisting of $-COOH$, $-SO_3H$, $-SO_2H$, $-P(O)(OR^{19})(OH)$, $-OP(O)(OR^{19})(OH)$, $-OSO_3H$, wherein R^{19} is selected from the group consisting of alkyl, substituted alkyl, aryl and substituted aryl; and~~

~~(b)~~ a group of the formula:

$$-M-Q^b-D'$$

wherein:

M is selected from the group consisting of $-CH_2OC(O)-$ and $-CH_2CH_2C(O)-$;

Q^b is a covalent bond or a linking group of formula:

$$-[E-(F^*)_n-G]_m-$$
$$\overset{O}{}$$

wherein:

m is an integer of from 1 to 4;

n is 0 or 1;

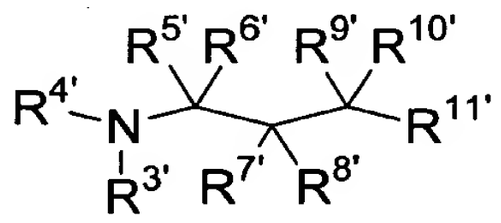
E is –NH- or –O-;

F* is selected from a group consisting of alkylene, substituted alkylene, alkenylene, substituted alkenylene, alkynylene, substituted alkynylene, cycloalkylene, substituted cycloalkylene, cycloalkenylene, substituted cycloalkenylene, arylene, substituted arylene, heteroarylene, substituted heteroarylene, heterocyclene and substituted heterocyclene; and

G is -OC(O)-, -C(O)- or –NH-;

wherein Q^b ~~which~~ is cleavable ~~may cleave~~ under physiological conditions ~~to release a GABA analog or active metabolite thereof into the systemic blood circulation of said animal~~; and

D' is a GABA analog moiety ~~preferably~~ of the formula:



wherein:

$R^{3'}$ is ~~selected from the group consisting of hydrogen, an amino protecting group, or~~ a covalent bond linking the GABA analog moiety to Q^b;

$R^{4'}$ is hydrogen or $R^{4'}$ and $R^{9'}$ together with the atoms to which they are attached form a heterocyclic ring;

$R^{5'}$ and $R^{6'}$ are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, aryl, substituted aryl, heteroaryl and substituted heteroaryl;

$R^{7'}$ and $R^{8'}$ are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, alkynyl, aryl, substituted aryl, heteroaryl and substituted heteroaryl, or $R^{7'}$ and $R^{8'}$ together with the atoms to which they are attached form a cycloalkyl, substituted cycloalkyl, heterocyclic or substituted heterocyclic ring;

$R^{9'}$ is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, alkynyl, aryl, substituted aryl, heteroaryl and substituted heteroaryl;

$R^{10'}$ is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, alkynyl, aryl, substituted aryl, heteroaryl and substituted heteroaryl;

$R^{11'}$ is selected from the group consisting of carboxylic acid, carboxylic amide, carboxylic ester, sulfonamide, phosphonic acid, acidic heterocycle, sulfonic acid, and hydroxamic acid ~~and C(O)$R^{12'}$~~;

~~$R^{12'}$ is a covalent bond linking the GABA analog moiety to Q^b, provided only one of $R^{3'}$ and $R^{12'}$ links D to Q^b;~~ or

a pharmaceutically acceptable salt thereof;

~~provided that when X is hydroxy, then Z is a group of the formula –M–Q^b–D';~~

~~and~~

~~further~~ provided that when X is hydroxy, M is $-CH_2CH_2C(O)-$, Q^b is a covalent bond and $R^{11'}$ is carboxylic acid, then at least one of $R^{5'}$, $R^{6'}$, $R^{7'}$, $R^{8'}$, $R^{9'}$ and $R^{10'}$ is other than hydrogen; and

~~yet~~ further provided that ~~neither Q^a nor~~ Q^b is not a linear oligopeptide comprised exclusively of 1, 2 or 3 α-amino acids and/or β-amino acids.

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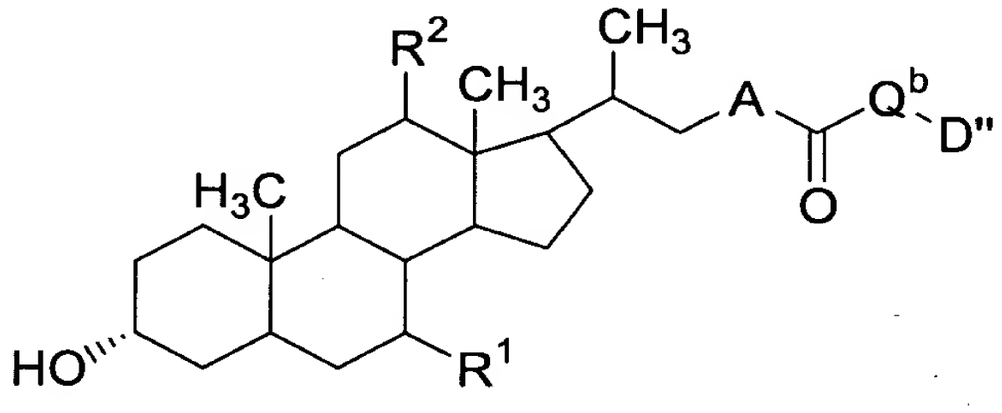
6. (Currently Amended) A compound of formula (II):



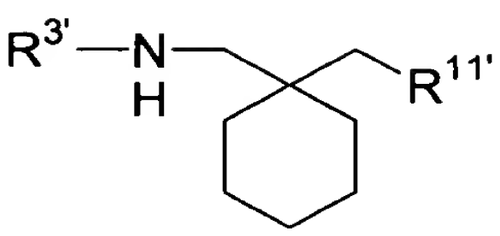
(II)

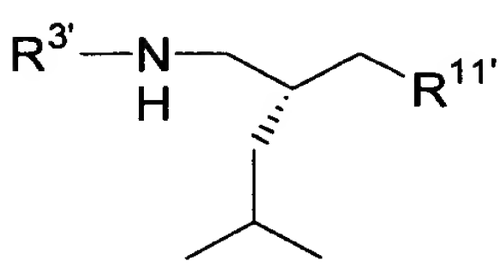
wherein:

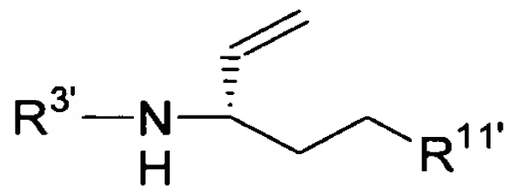
R^1 and R^2 are both α-OH; or R^1 is β-OH and R^2 is hydrogen; or R^1 is α-OH and R^2 is hydrogen; or R^1 is hydrogen and R^2 is α-OH; or R^1 is β-OH and R^2 is α-OH; or R^1 and R^2 are both hydrogen;

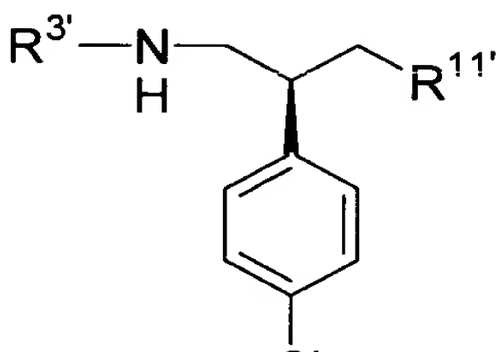
A is –O– or $-CH_2-$;

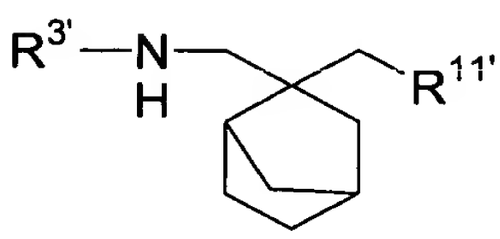
D'' is a GABA analog moiety selected from the group consisting of:

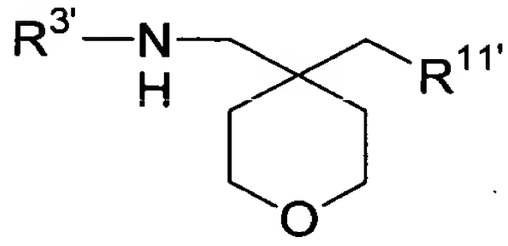












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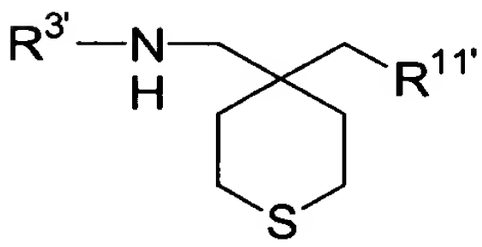

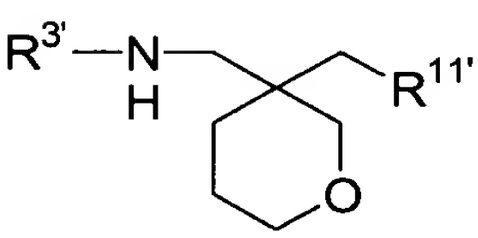

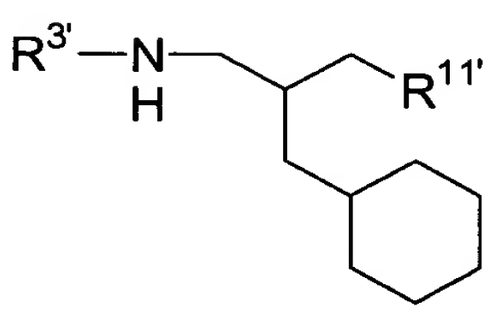

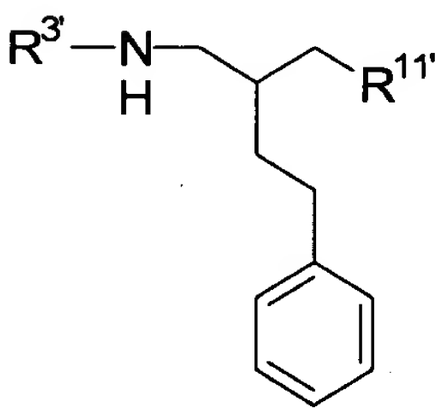

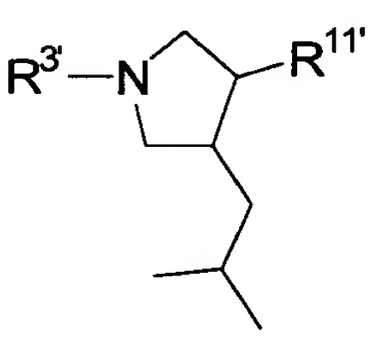

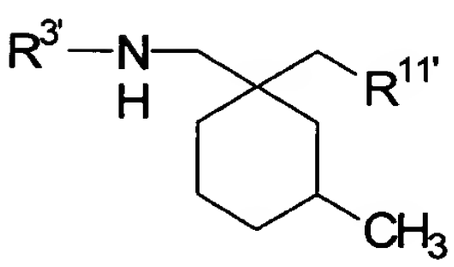

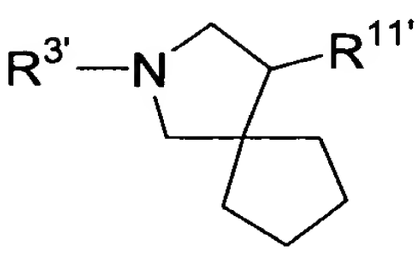

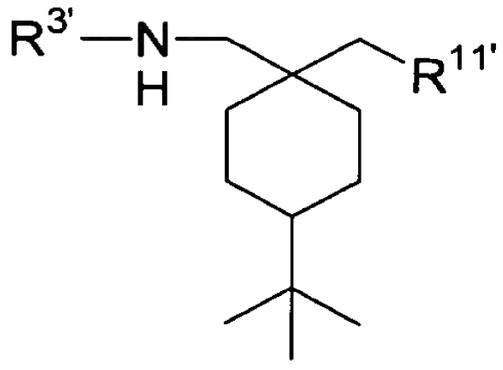

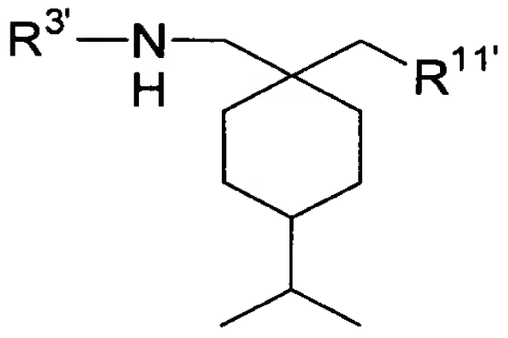

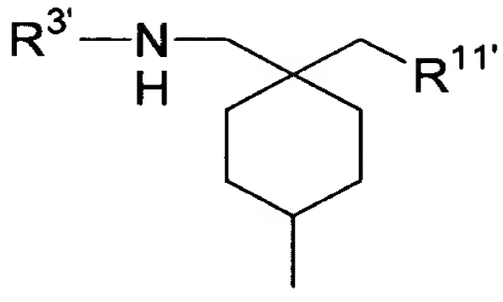
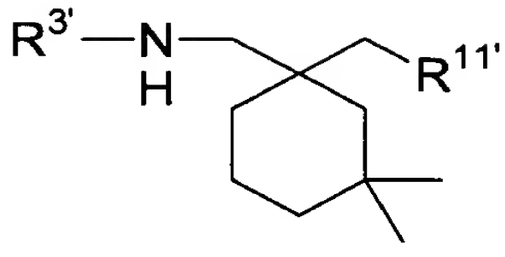
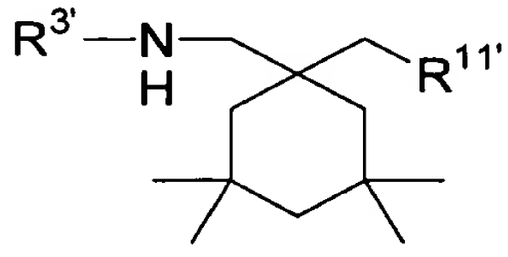
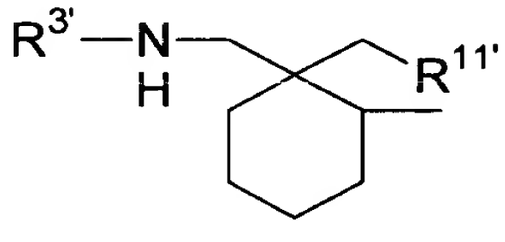
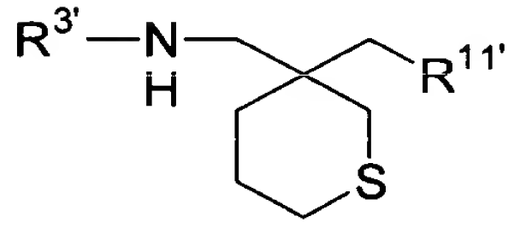
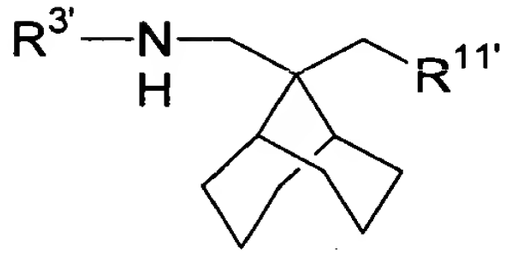

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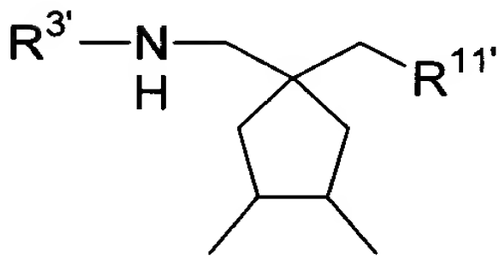
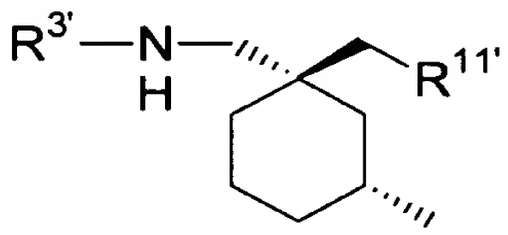
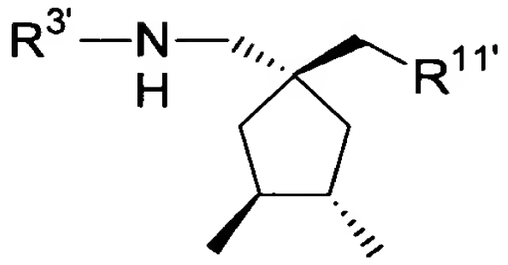
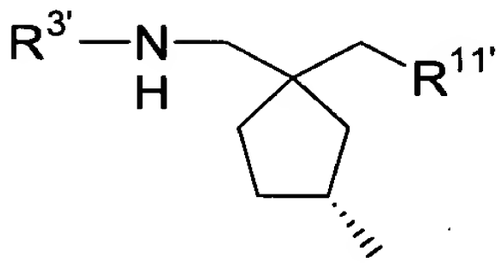
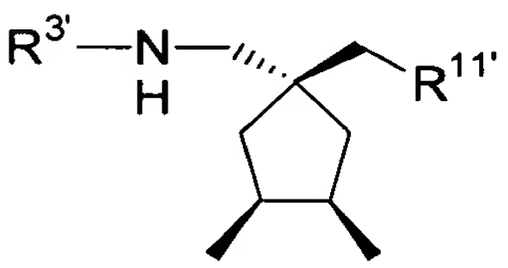
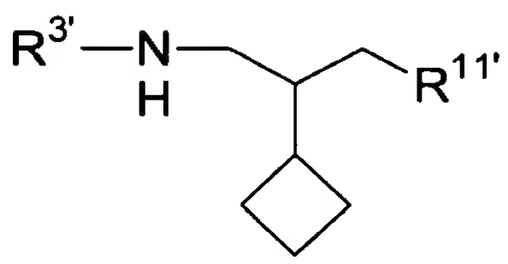
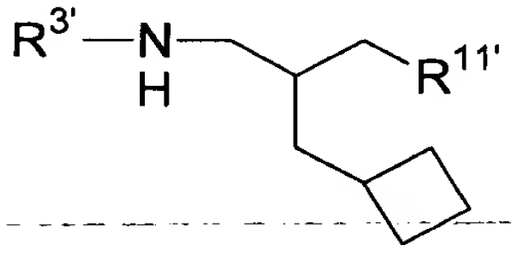
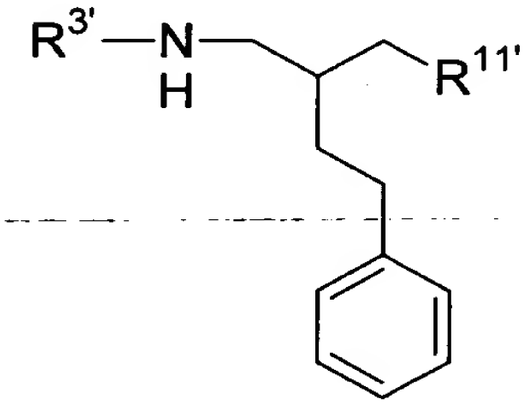
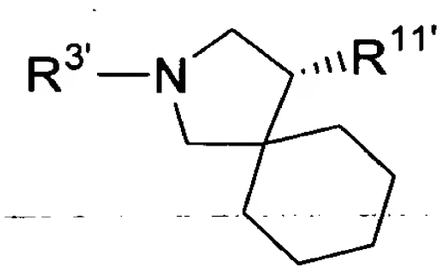










where

$R^{3'}$ is ~~hydrogen or~~ a covalent bond linking D" to Q^b;

$R^{11'}$ is carboxyl acid ~~or C(O)$R^{12'}$, wherein $R^{12'}$ is a covalent bond linking D" to Q^b~~; and

Q^b is a covalent bond or a linker of the following formula:

$$-[E-(F^*)_n-G]_m-$$

wherein:

m is an integer of from 1 to 4;

n is 0 or 1;

E is –NH- or –O-;

F* is selected from a group consisting of alkylene, substituted alkylene, alkenylene, substituted alkenylene, alkynylene, substituted alkynylene, cycloalkylene, substituted cycloalkylene, cycloalkenylene, substituted cycloalkenylene, arylene, substituted arylene, heteroarylene, substituted heteroarylene, heterocyclene and substituted heterocyclene; and

G is -OC(O)-, -C(O)- or –NH-;

wherein Q^b ~~which~~ is cleavable ~~may cleave~~ under physiological conditions ~~to release a GABA analog or an active metabolite thereof thereby providing a therapeutic or prophylactic systemic blood concentration of said GABA analog or an active metabolite thereof in said animal, wherein said linker~~ provided that Q^b is not a linear oligopeptide consisting of 1, 2 or 3 α-amino acids and/or β-amino acids; or

a pharmaceutically acceptable salt thereof;

Cl cont.

~~7. (Currently Amended) The compound according to Claim 6, wherein Q^b is a linker covalent bond.~~

8. (Currently Amended) The compound according to Claim 6 ~~7~~, wherein Q^b is the ~~a~~ group of formula:

$-[E-(F^*)_n-G]_m-$

~~wherein:~~

~~m is an integer of from 1 to 4;~~

~~n is 0 or 1;~~

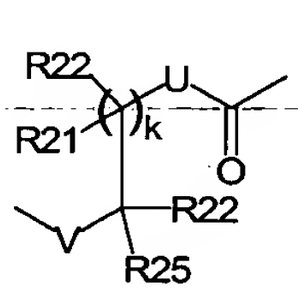
~~E is –NH– or –O–;~~

~~F* is selected from a group consisting of alkylene, substituted alkylene, alkenylene, substituted alkenylene, alkynylene, substituted alkynylene, cycloalkylene, substituted cycloalkylene, cycloalkenylene, substituted cycloalkenylene, arylene, substituted arylene, heteroarylene, substituted heteroarylene, heterocyclene and substituted heterocyclene; and~~

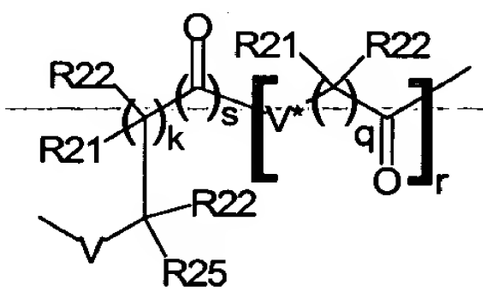
~~G is –OC(O)–, –C(O)– or –NH–~~.

9. (Currently Amended) The compound according to Claim 6 ~~8~~, wherein F* is selected from a group consisting of alkylene, alkynylene and alkylene substituted with a group selected from the group consisting of –COOH, $-SO_3H$, $-SO_2H$, $-P(O)(OR^{19})(OH)$, $-OP(O)(OR^{19})(OH)$, $-OSO_3H$, wherein R^{19} is selected from the group consisting of alkyl, substituted alkyl, aryl and substituted aryl; and where one, two or three methylene groups are optionally replaced by a carboxy (-C(O)O-) group.

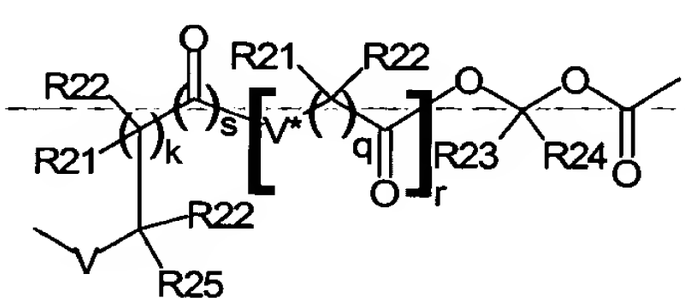
10. (Currently Amended) The compound according to Claim 6 ~~7~~ wherein Q^b is a cleavable linker selected from the group consisting of structures of formulae (vi) to (viii) ~~(x)~~:



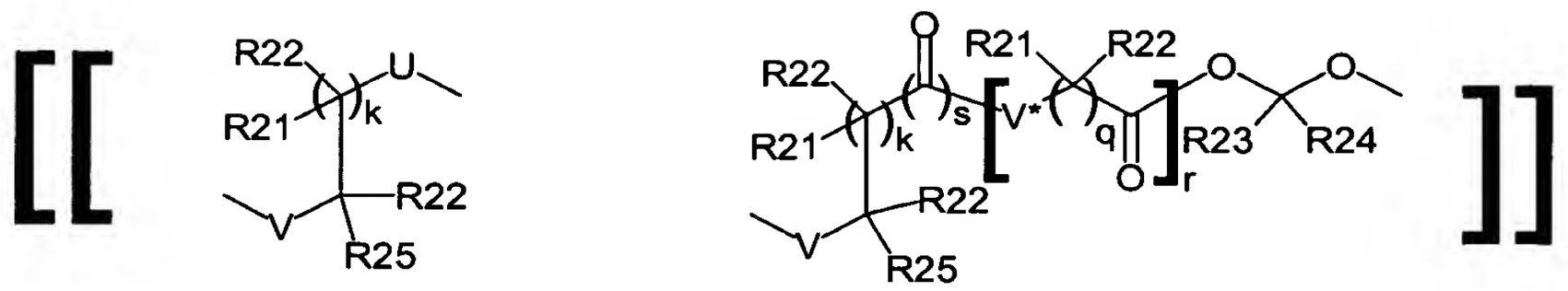
(vi)



(vii)



(viii)



(ix) (x)

wherein:

V and V* are independently ~~NR^{20};~~ ~~–~~NH- or O~~, S or CR^{21}R^{22}~~;

U is ~~NR^{20};~~ O~~, S~~;

R^{25} is R^{21} or $(CR^{21}R^{22})_lZ$;

Z is selected from the group consisting of $-CO_2H$, $-SO_3H$, $-OSO_3H$, $-SO_2H$, $-P(O)(OR^{19})(OH)$, $-OP(O)(OR^{19})(OH)$;

s is ~~0 or~~ 1;

r is 0, 1 or 2;

k is 0, 1, 2, 3 or 4;

each q is 1, 2, 3 or 4;

l is 0 or 1;

~~R^{19} is selected from the group consisting of alkyl, substituted alkyl, substituted aryl and substituted aryl;~~

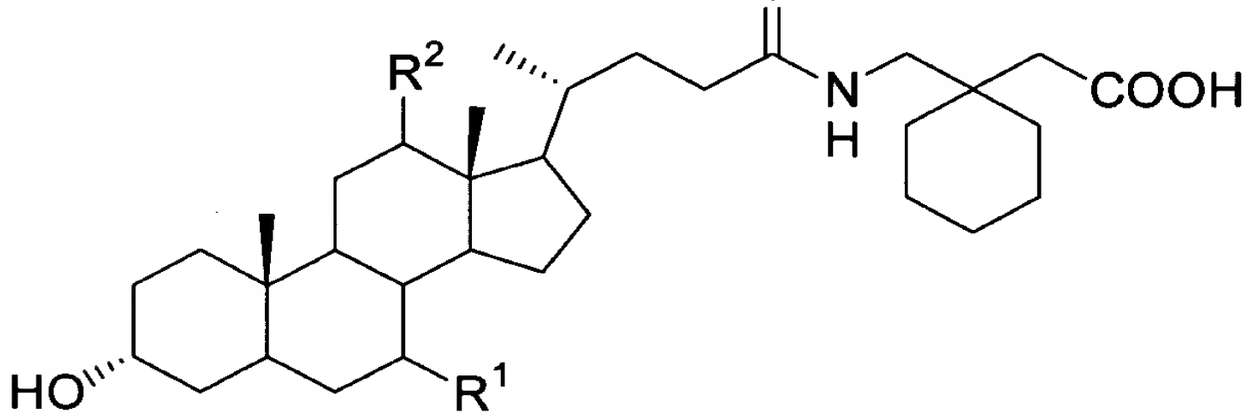
~~R^{20}~~, R^{21} and R^{22} are independently hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl or R^{21} and R^{22} together with the atoms to which they are attached form a cycloalkyl, substituted cycloalkyl, heterocyclyl or substituted heterocyclyl ring, or, when R^{20} and R^{22} are present and are on adjacent atoms, then together with the atoms to which they are attached form a heterocyclyl or substituted heterocyclyl ring;

R^{23} and R^{24} are independently hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl or R^{23} and R^{24} together with the atoms to which they are attached form a cycloalkyl, substituted cycloalkyl, heterocyclyl or substituted heterocyclyl ring;

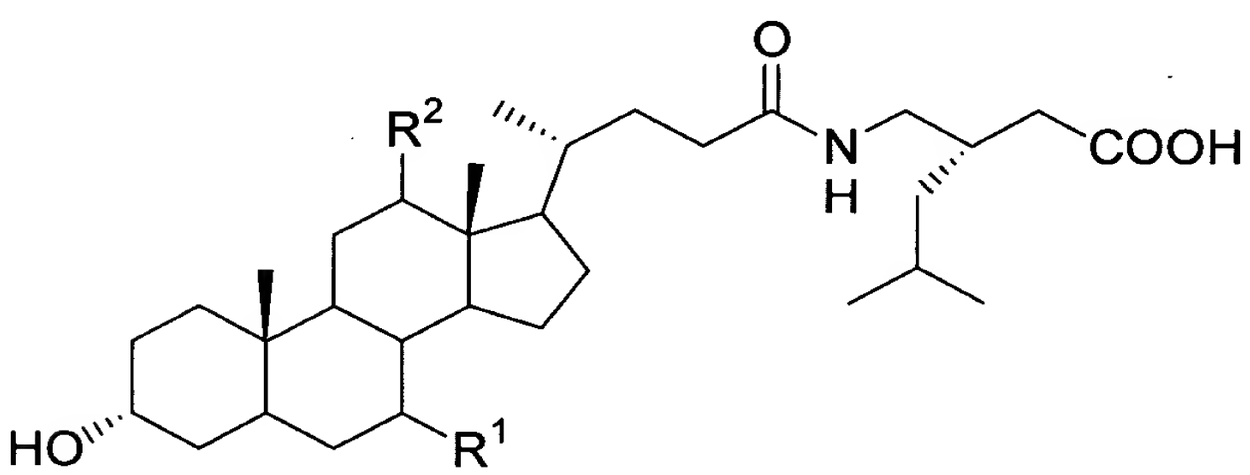
provided that when Q^b is of formula (vii), V and V* are –NH- ~~NR^{20}~~, s is 1, k is 0 or 1, each q is either 1 or 2, and r is 0, 1 or 2 then R^{25} is Z.

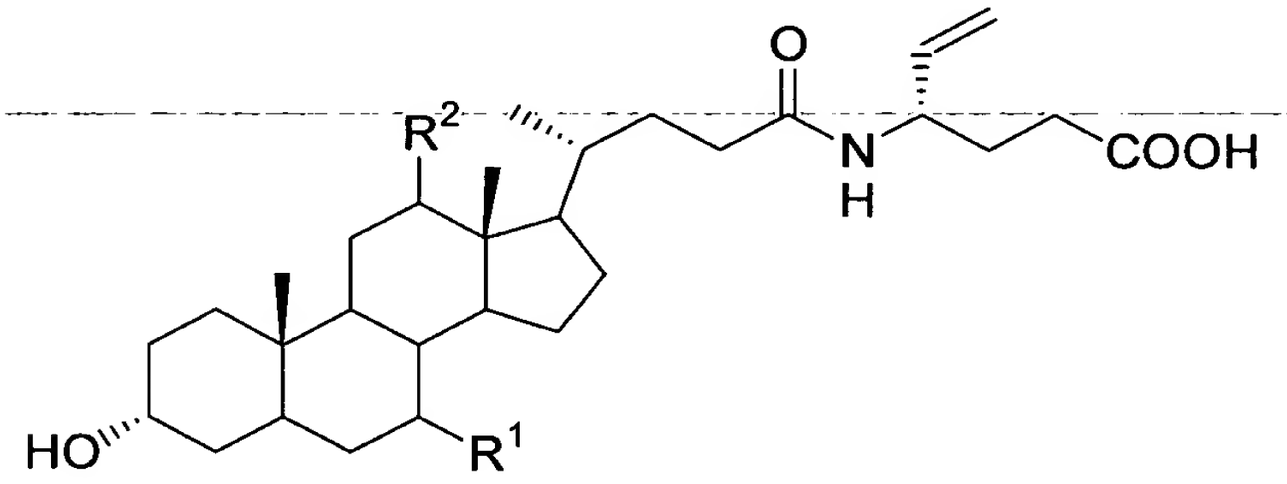
11 – 17. (Canceled)

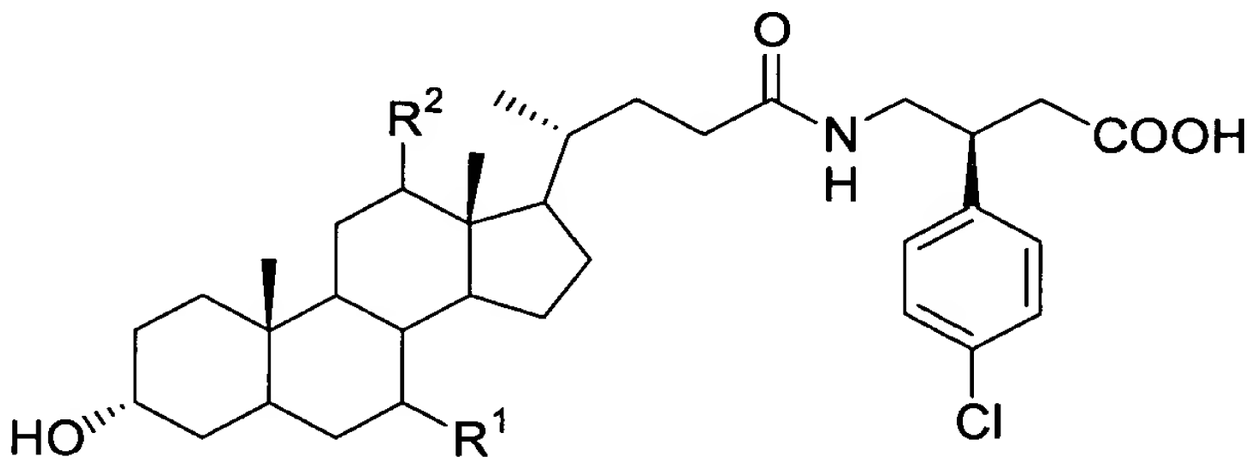
18. (Original) A compound selected from the group consisting of:

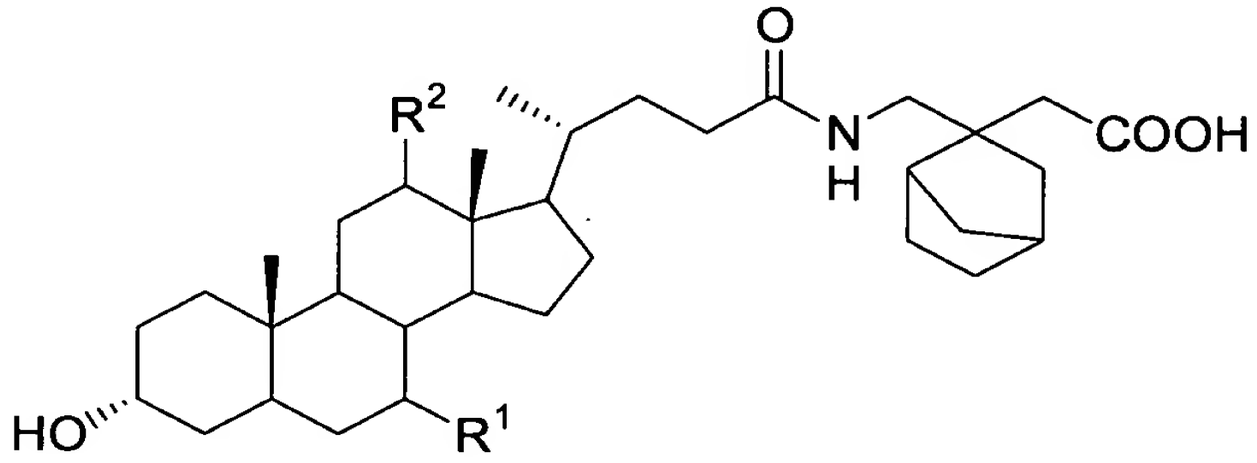


Al cont.

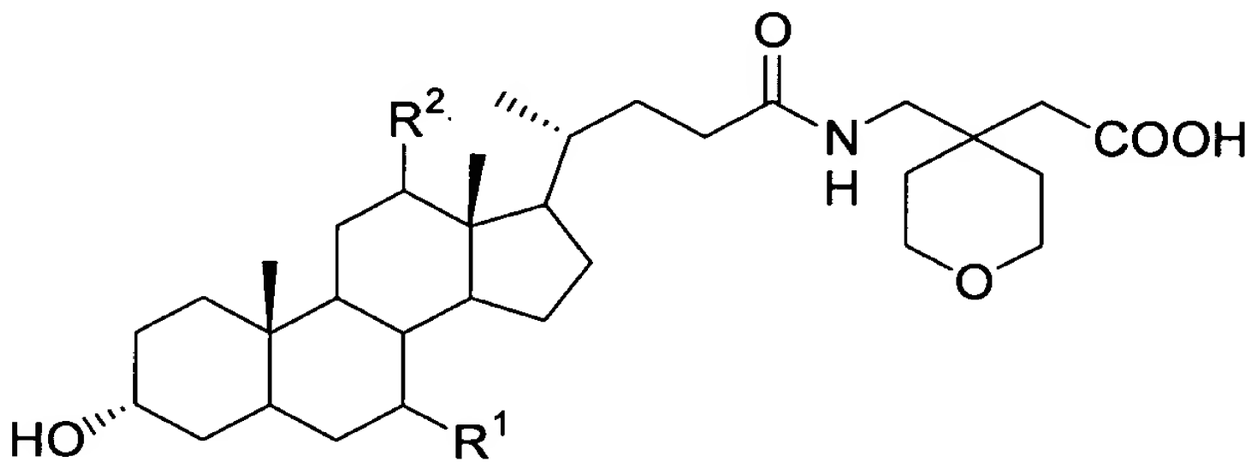


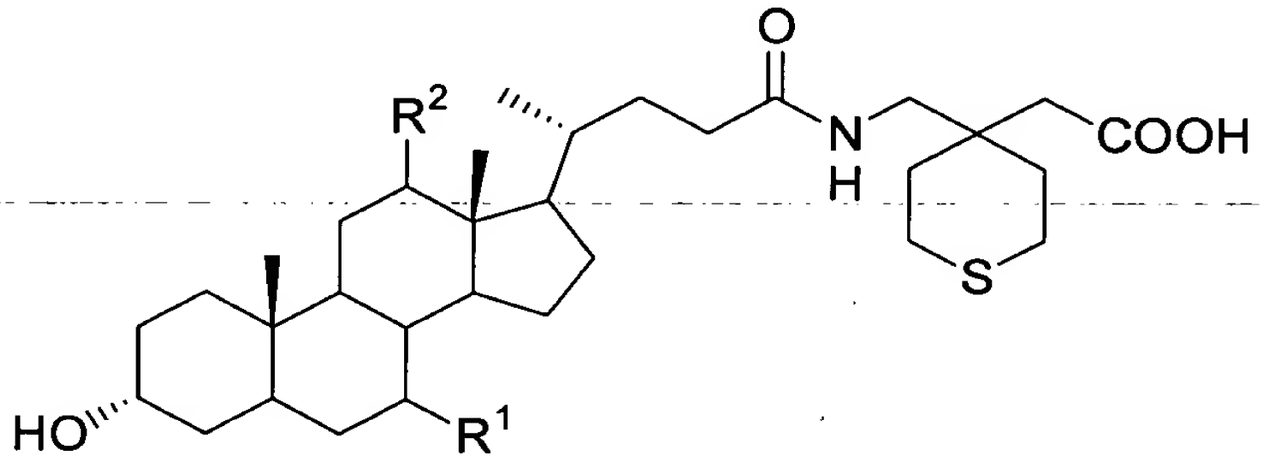


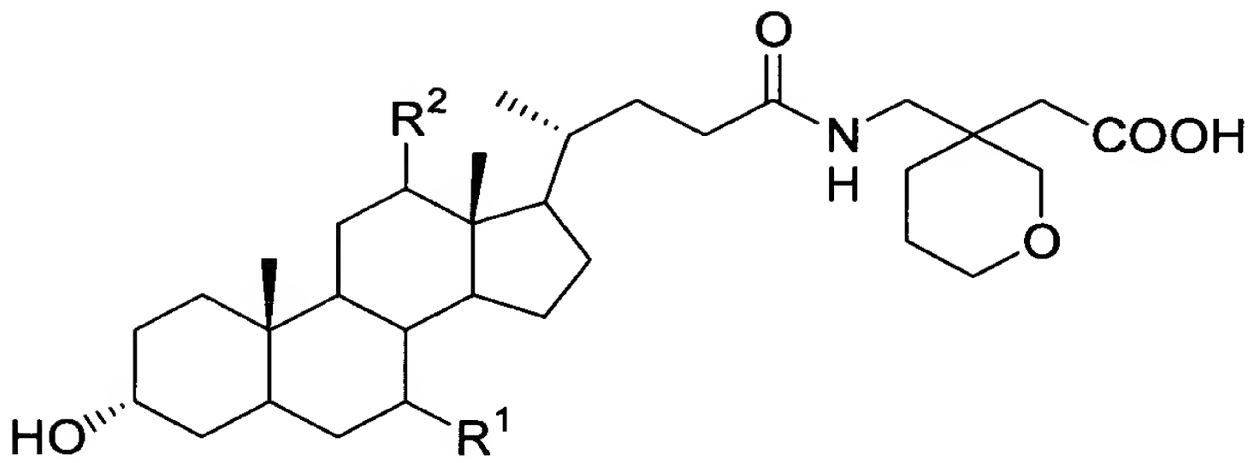

O
R2
N
H
COOH
HO
R1
Cl

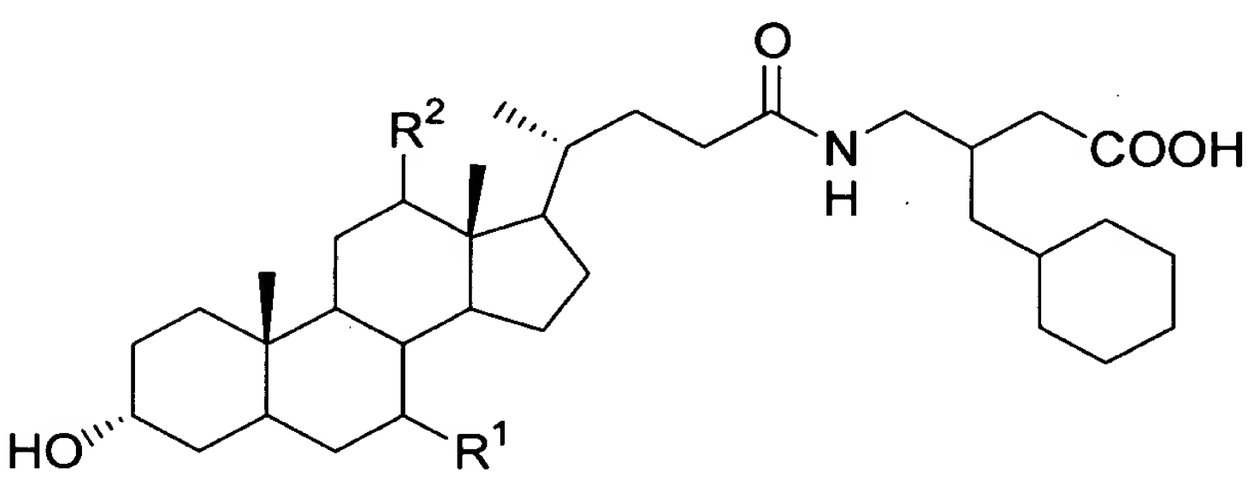

O
R2
N
H
COOH
HO
R1

Al cont'

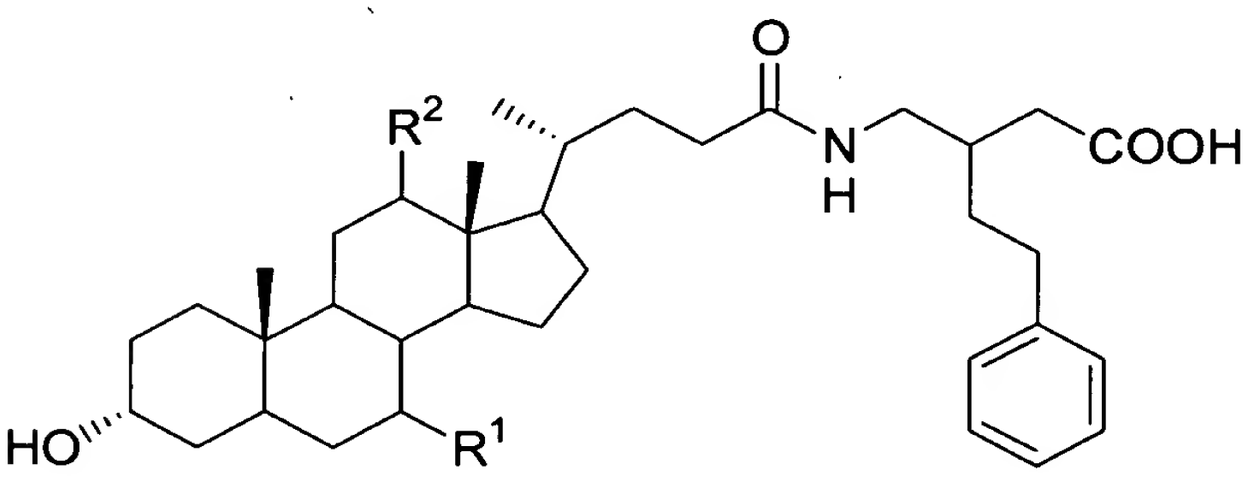

O
R2
N
H
COOH
O
HO
R1

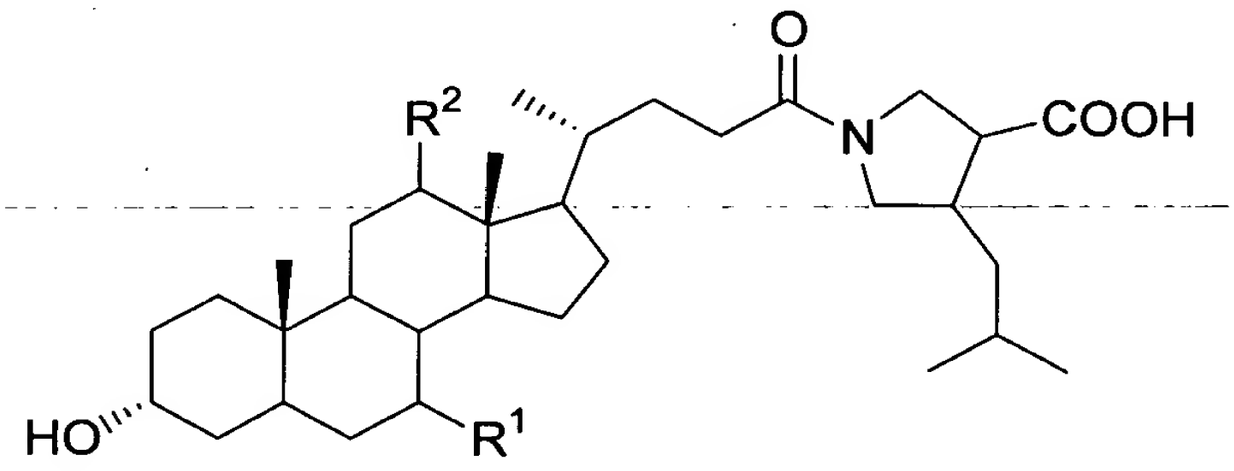

O
R2
N
H
COOH
S
HO
R1

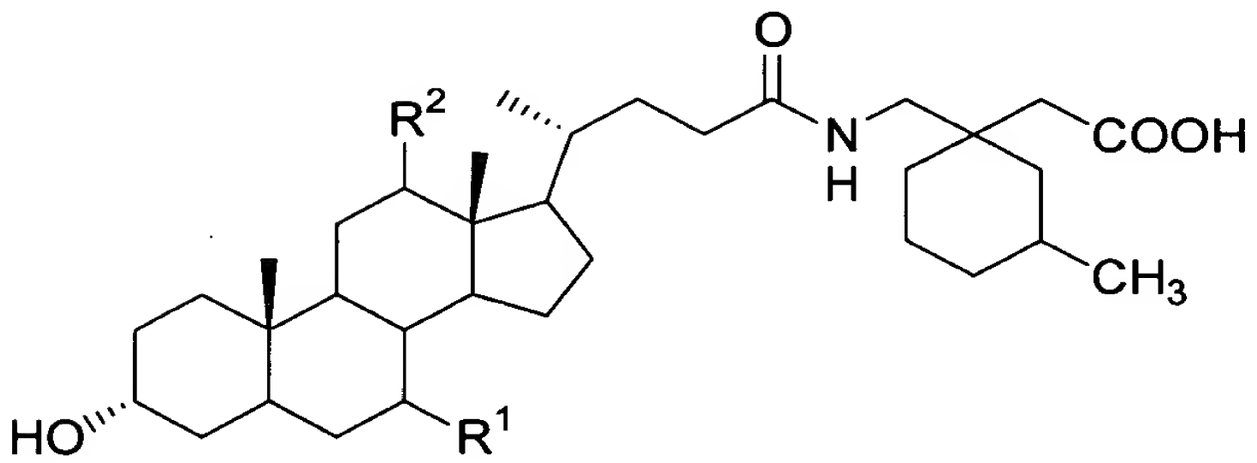


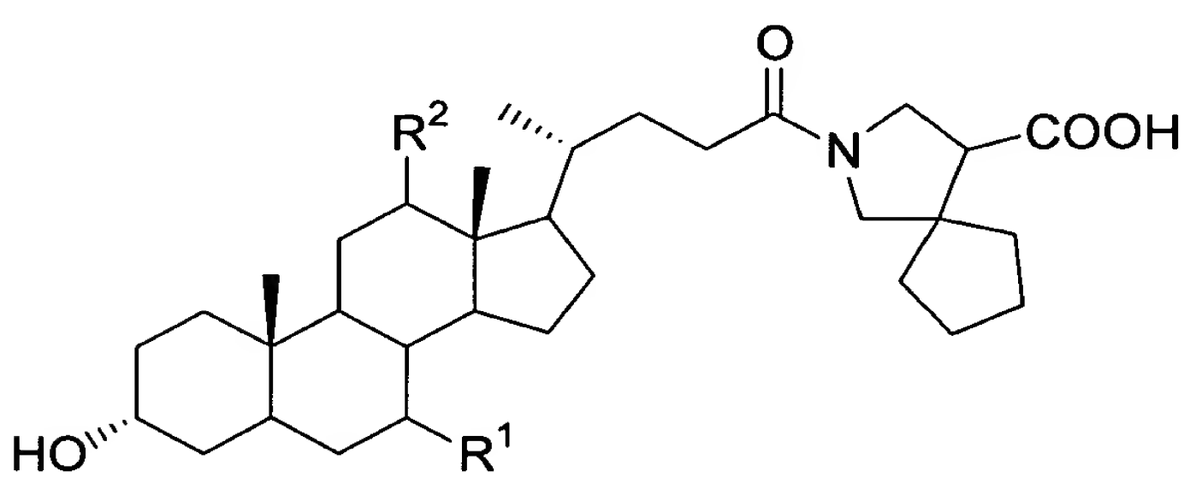


Al cont.

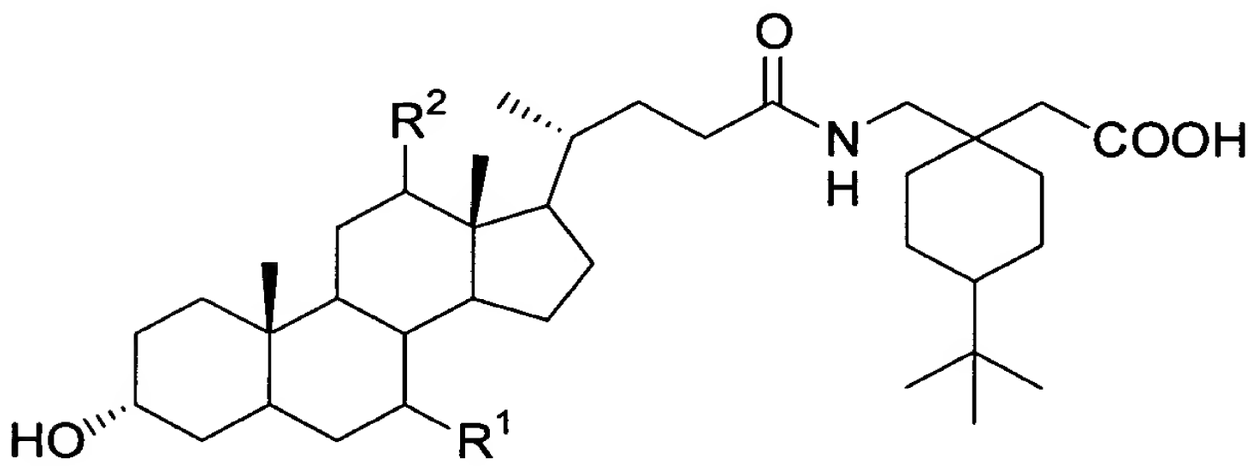


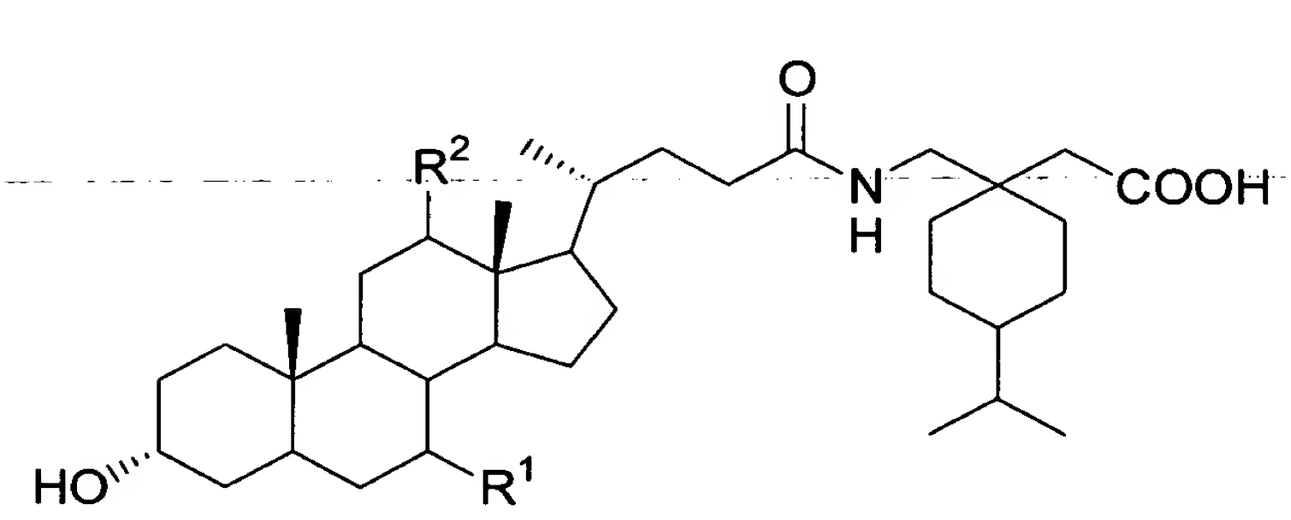


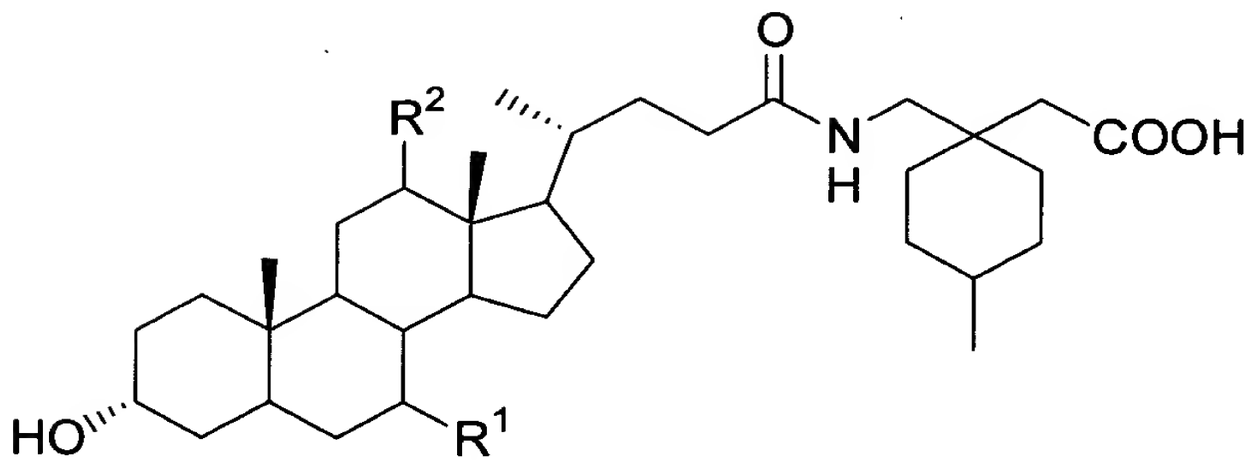

O
R2
N
H
COOH
CH3
HO
R1

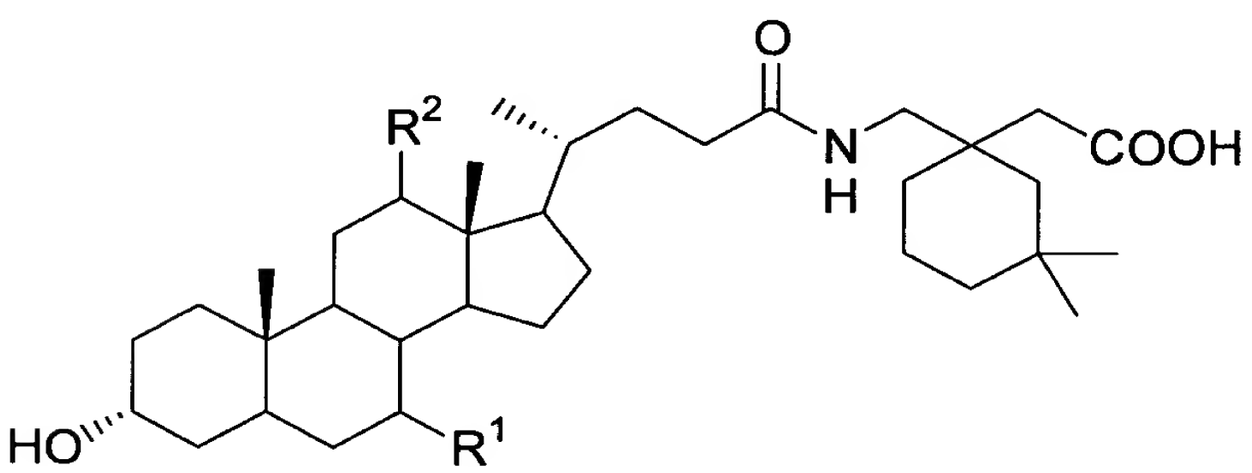

O
R2
N
COOH
HO
R1

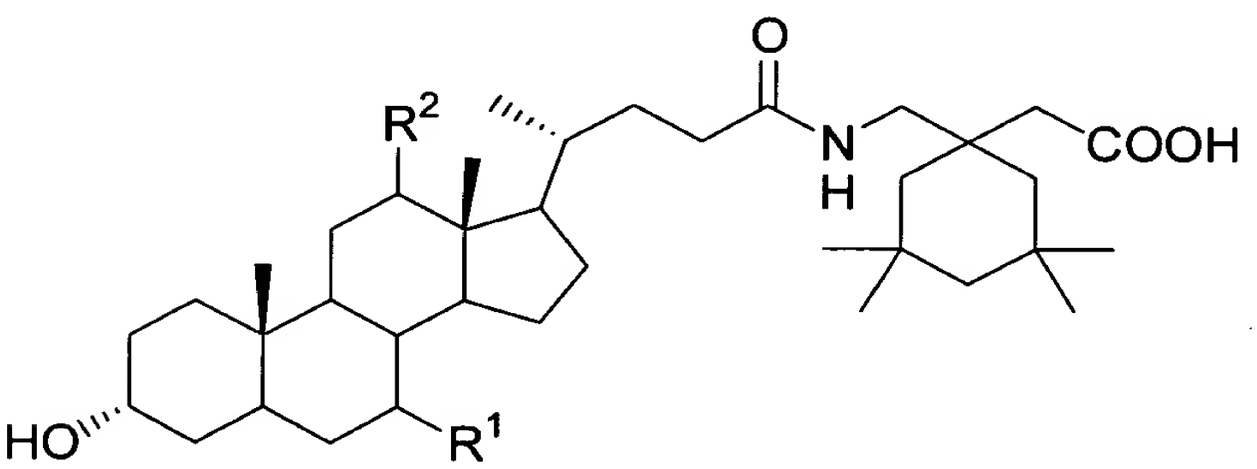
a
cont'd

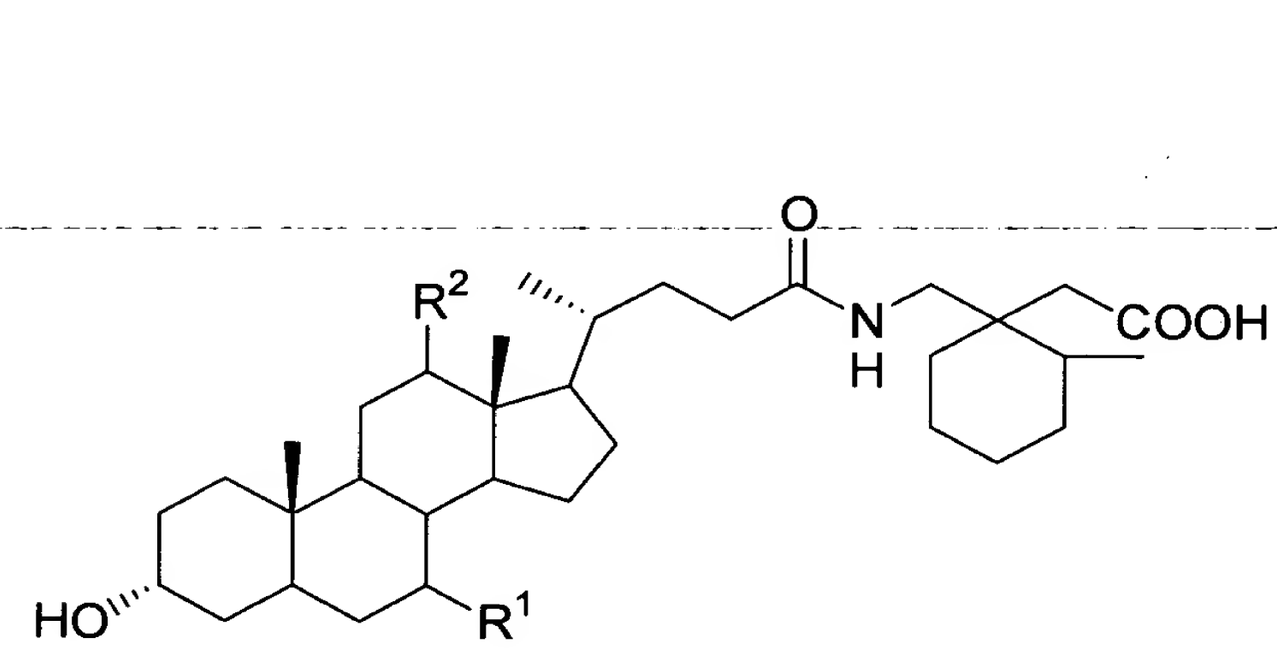

O
R2
N
H
COOH
HO
R1

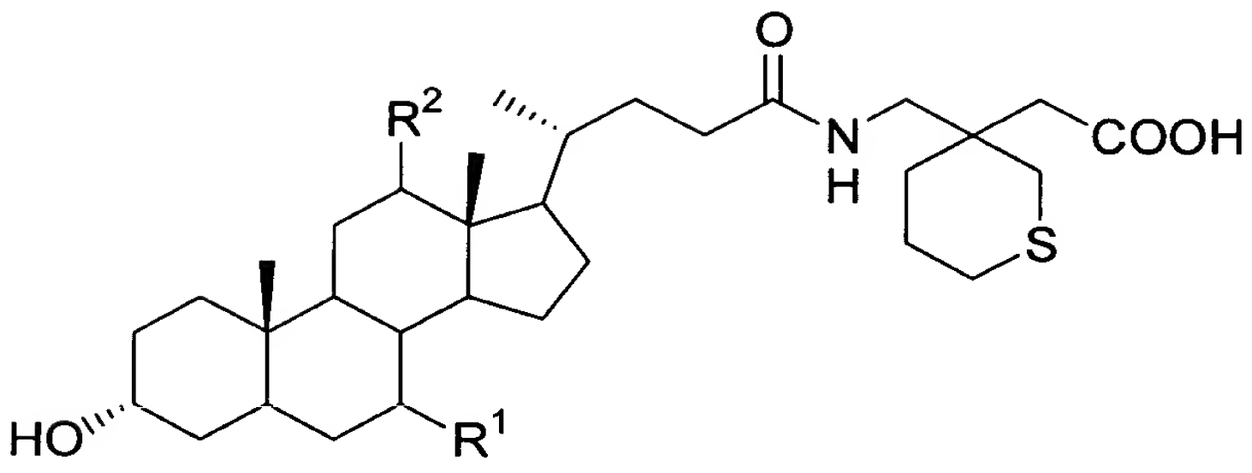

O
R2
N
H
COOH
HO
R1


O
R2
N
H
COOH
HO
R1

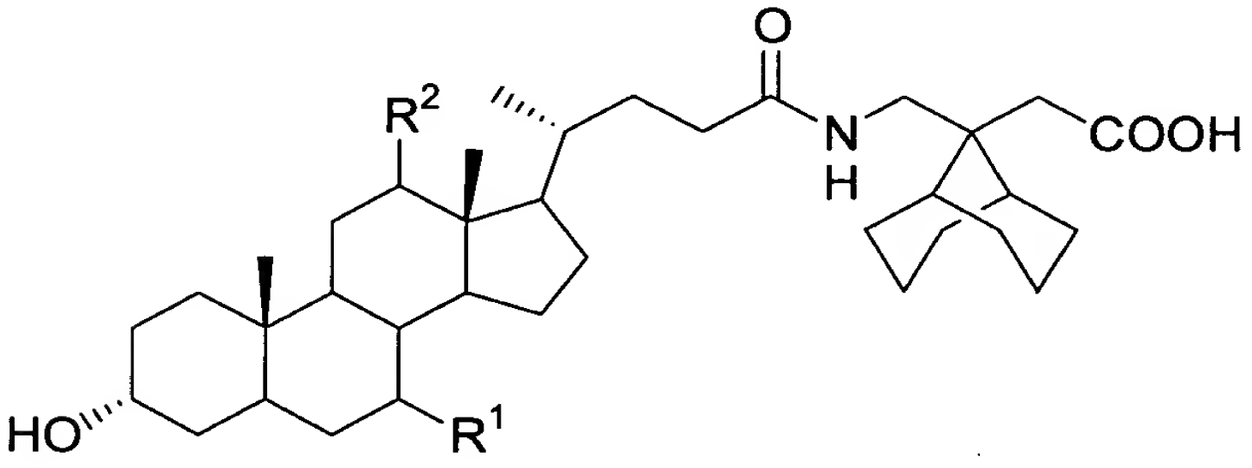

O
R2
N
H
COOH
HO
R1

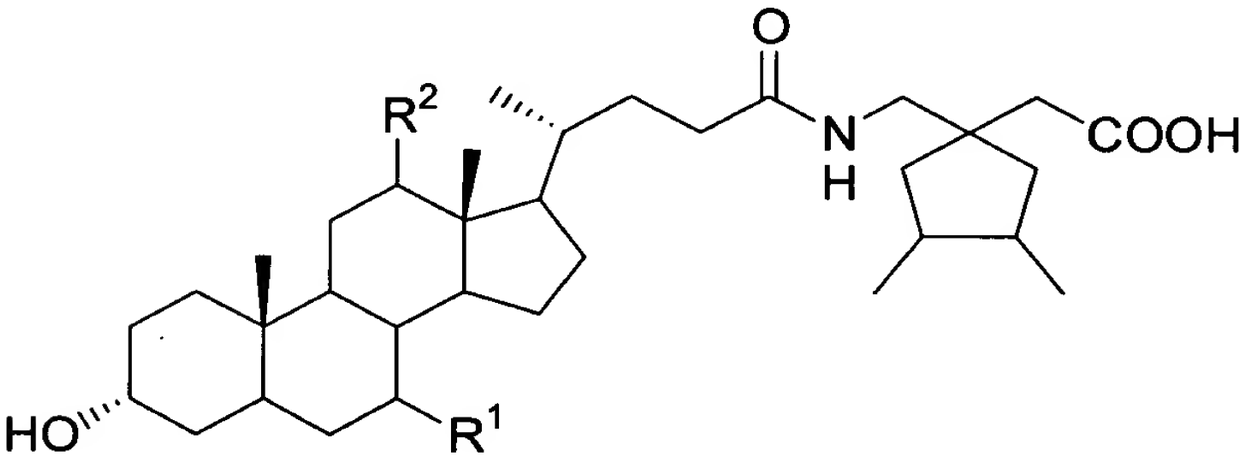

O
R2
N
H
COOH
HO
R1

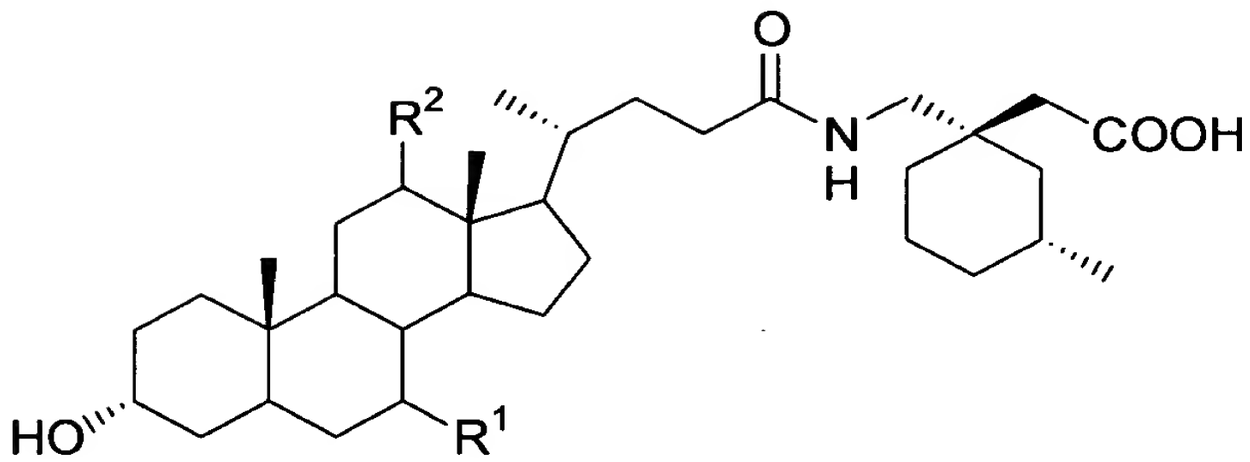

O
R2
N
H
COOH
HO
R1

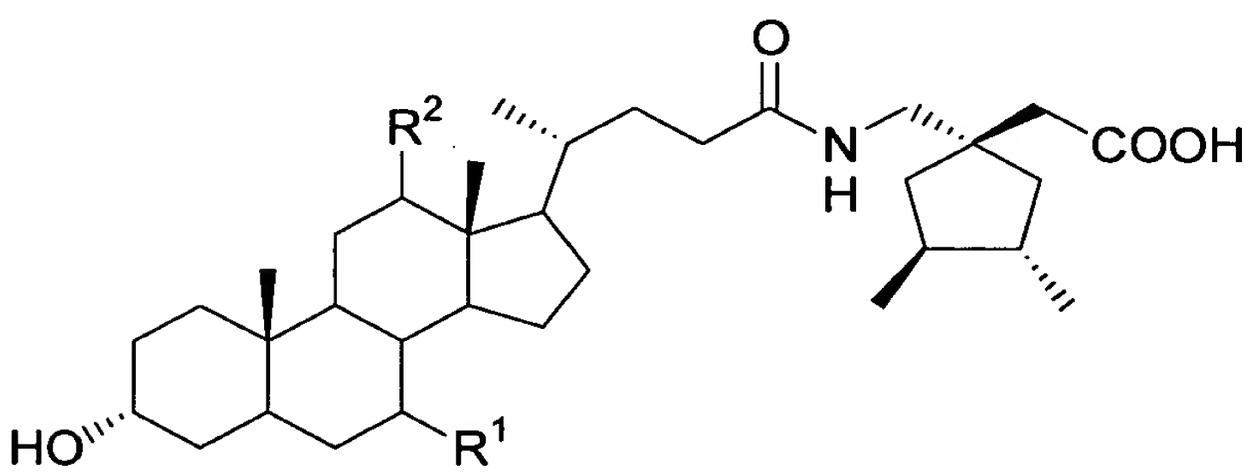


a1 cont'

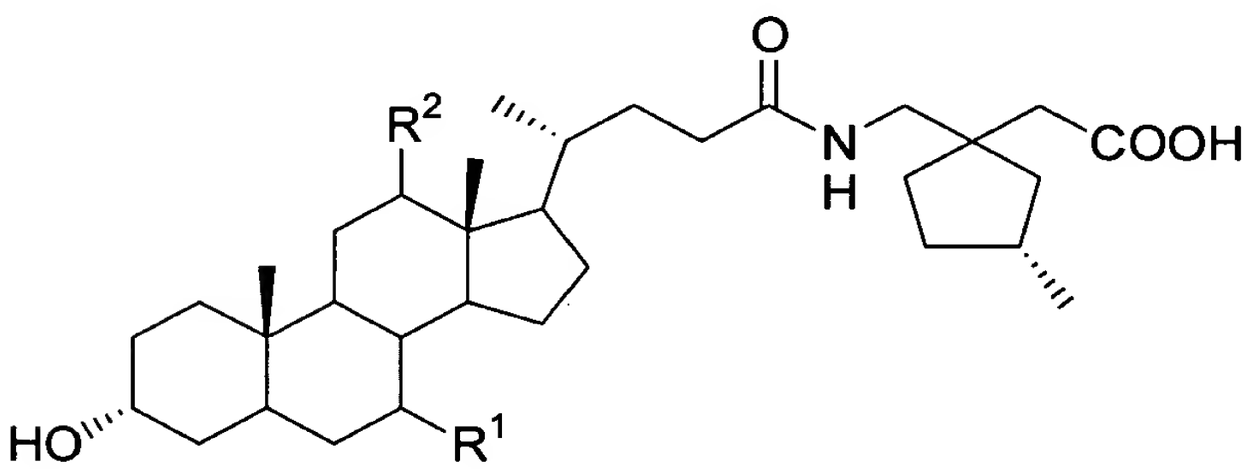


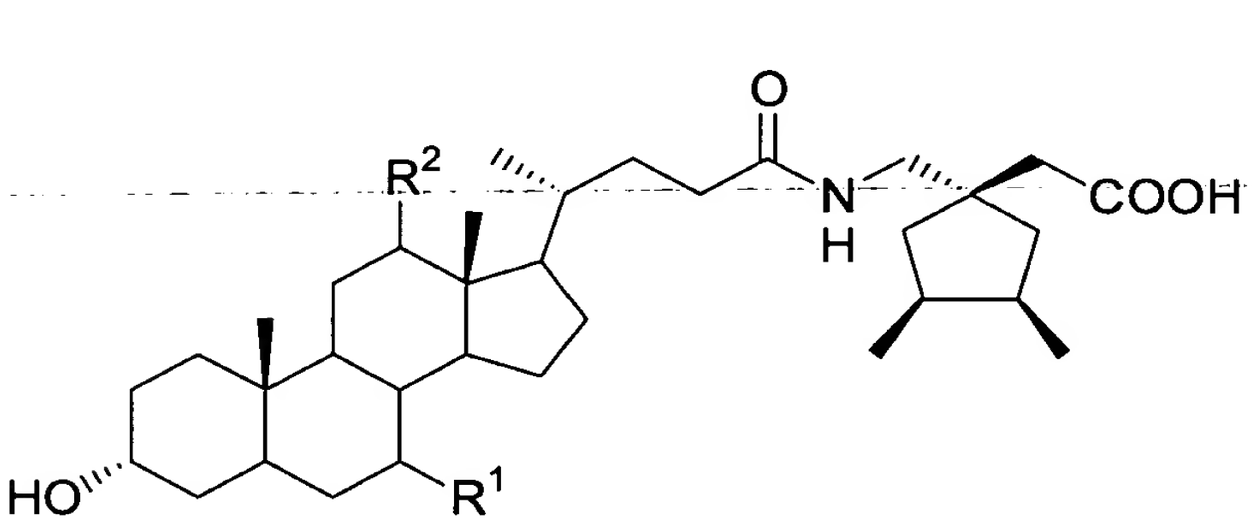


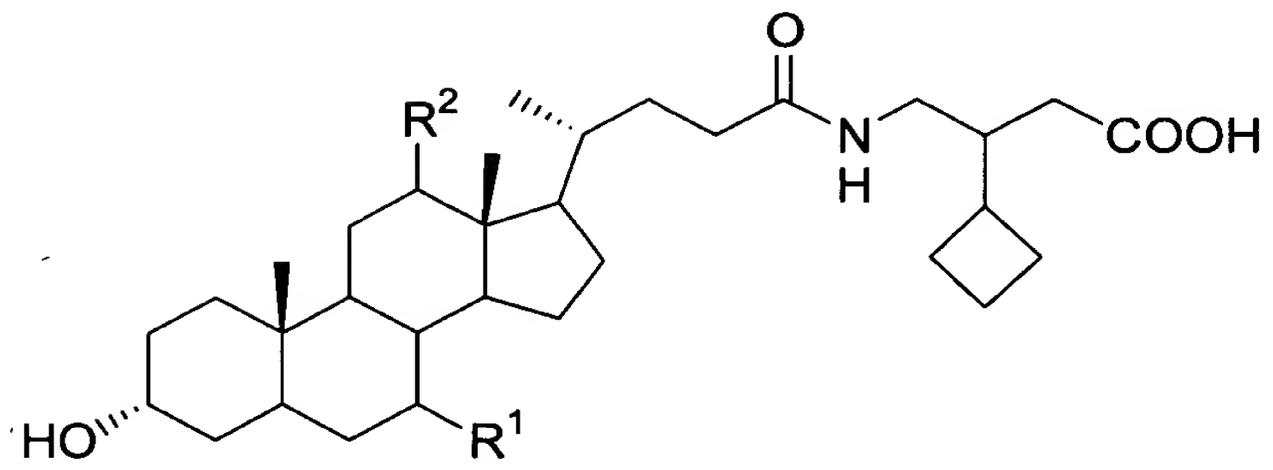

O
R2
N
H
COOH
HO
R1


O
R2
N
H
COOH
HO
R1

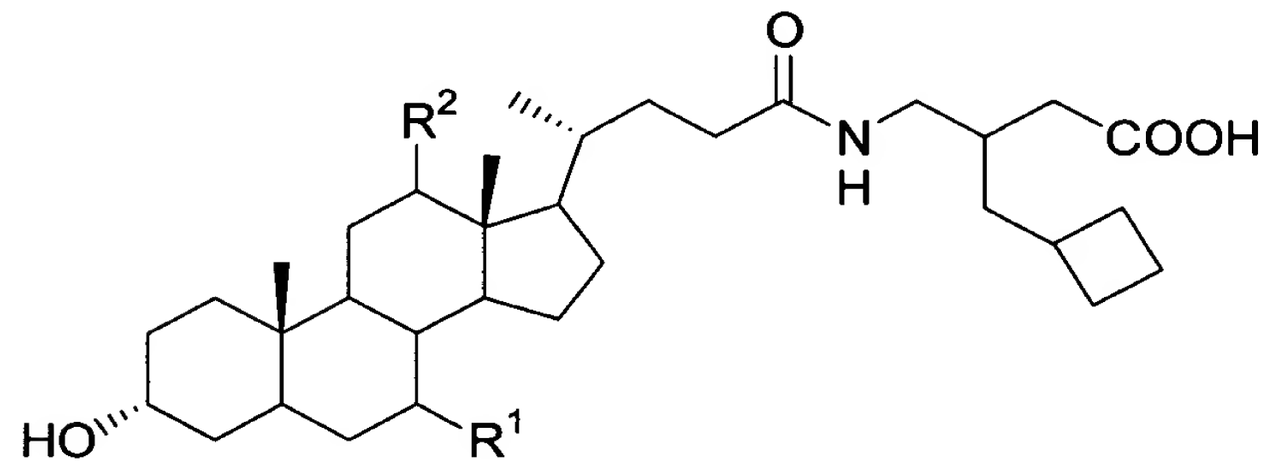
a1 cont.

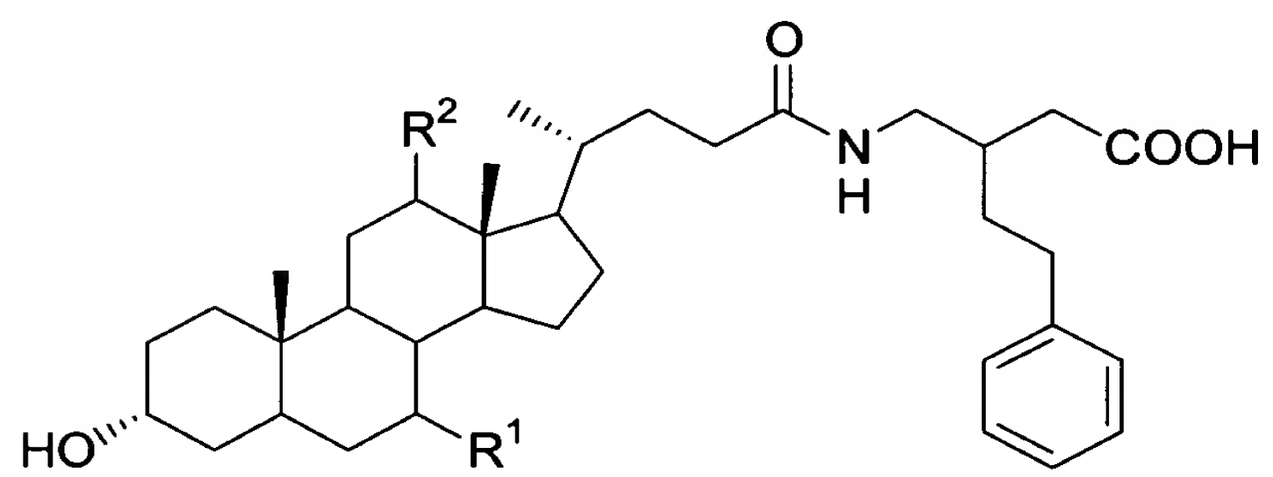

O
R2
N
H
COOH
HO
R1

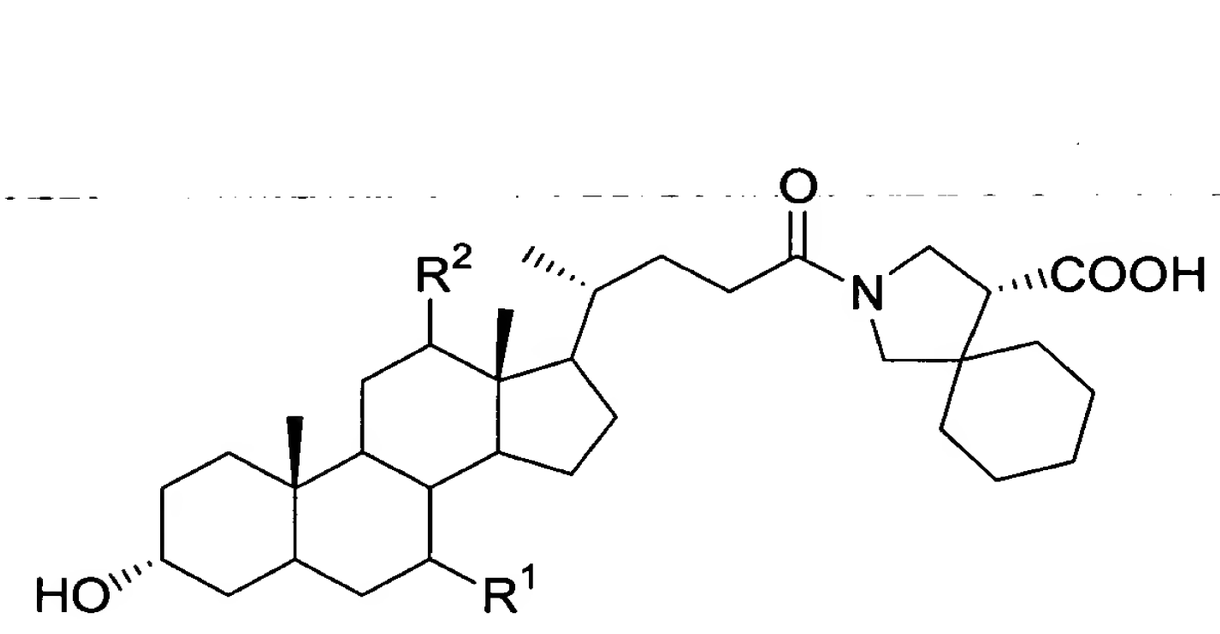

O
R2
N
H
COOH
HO
R1


O
R2
N
H
COOH
HO
R1

A'
Cont.


O
R2
N
H
COOH
HO
R1


O
R2
N
H
COOH
HO
R1


O
R2
N
COOH
HO
R1

where R^1 and R^2 are independently hydrogen or hydroxy; or

pharmaceutically acceptable salts thereof.

19. (Currently Amended) A pharmaceutical composition comprising a pharmaceutically acceptable excipient and a compound according to any of Claims ~~1,~~ 5, 6, ~~11, 15,~~ or 18.

Allowed

20. (Original) A method for treating a disease condition in a mammal, wherein said disease condition is selected from epilepsy, faintness attacks, hypokinesia, cranial disorders, neurodegenerative disorders, depression, anxiety, panic, pain, neuropathic pain, neuropathological disorders, gastrointestinal damage, inflammation and irritable bowel disease, which method comprises administering to said mammal a pharmaceutical composition according to Claim 19.